UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,982	04/02/2007	Robin Kurfurst	15675P620	2408

7590 06/16/2010

Blakely, Sokoloff, Taylor & Zafman
12400 Wilshire Boulevard, 7th floor
Los Angeles, CA 90025

EXAMINER	
GIBBS, TERRA C	
ART UNIT	PAPER NUMBER
1635	
MAIL DATE	DELIVERY MODE
06/16/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,982	KURFURST ET AL.	
	Examiner	Art Unit	
	TERRA C. GIBBS	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38,42-57 and 60-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38,42-57 and 60-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *May 18, 2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission mailed on May 18, 2010 has been entered.

New claim 67 is acknowledged.

Claims 38, 42-57, and 60-67 are pending in the instant application.

Claims 38, 42-57, and 60-67 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Applicant's Amendment and Response filed May 18, 2010 have been considered. Rejections and/or objections not reiterated from the previous Office Action mailed November 18, 2009 are hereby withdrawn. Any arguments addressing said rejections and/or objections are moot. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Information Disclosure Statement

Applicant's information disclosure statement filed May 18, 2010 is acknowledged. The submission is in compliance with the provisions of 37 CFR §1.97. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

Claim Rejections - 35 USC § 103

In the previous Office Action mailed November 18, 2009, claims 38 and 42-57 were rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/02069 A1 ('069) (submitted and made of record on Applicant's Information Disclosure Statement filed November 20, 2006) as evidenced by Lazou et al. (submitted and made of record in the Office Action filed February 5, 2008). **This rejection is withdrawn** in view of the new 35 U.S.C. 103(a) presented below:

In the previous Office Action mailed November 18, 2009, claims 60-66 were rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/02069 A1 (submitted and made of record on Applicant's Information Disclosure Statement filed November 20, 2006) as evidenced by Park et al. (Journal of Biological Chemistry, 1993 Vol. 268:16:11742-11749, submitted and made of record on Applicant's Information Disclosure Statement filed November 20, 2006). **This rejection is withdrawn** in view of the new 35 U.S.C. 103(a) presented below:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 38, 42-57, and 60-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/02069 A1, also referred to as "Bennett" (submitted and made of record on Applicant's Information Disclosure Statement filed November 20, 2006) in view of Park et al. (Journal of Biological Chemistry, 1993 Vol. 268:16:11742-11749, submitted and made of record on Applicant's Information Disclosure Statement filed November 20, 2006).

Claim 38 is drawn to a method of depigmenting or bleaching human skin, body hair and/or hair of a head of a subject to lighten a color for purely cosmetic purposes comprising topical application to the skin, the body hair and/or the hair of the head of said subject of a cosmetic composition comprising at least one oligonucleotide having

between 7 and 25 nucleotides, capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 (PKC beta-l). Claims 42-56 and 60-67 are dependent on claim 38 and include all the limitations of claim 38 with the further limitations wherein said composition comprises at least one oligonucleotide capable of specifically hybridizing with any 5' to 3' regions, coding or non-coding region of genes coding for PKC beta-1; wherein said composition comprises SEQ ID NO:1 of Applicant's invention; wherein said composition comprises chemical modifications including modified sugar moieties of 2'-O-fluoro substituents; wherein said composition comprises a phosphodiester groups; wherein the phosphodiester groups are replaced by phosphorothioate groups; wherein the phosphodiester groups are replaced by methylphosphonate groups; wherein said composition comprises a vector or plasmid; wherein said composition comprises one or more active agents, including anti-inflammatory agents; wherein the oligonucleotide represents 0.00001% to 10% of the total weight of the composition; wherein said composition is presented in the form of an emulsion containing an oil; wherein the topical application comprises application of the composition to the hair of the head or the face; wherein the application of the composition comprises application of a makeup; wherein the composition comprises an SPF protective fluid; wherein the composition further comprises at least one additional active agent that is a depigmenting substance; wherein the active agent is selected from substances that inhibit the activity of tyrosinase; and wherein the topical application to the skin, the body hair and/or the hair of the head does not comprise skin having psoriasis or skin cancer. Claim 57 is drawn to a method for the treatment of regional

hyper-pigmentation by melanocyte hyperactivity such as idiopathic melasma, local hyper-pigmentation by benign melanocyte hyperactivity and proliferation such as pigmentary age spots, accidental hyper-pigmentation such as post-lesion healing in a subject in need thereof, comprising the topical application to the hyperpigmented skin areas of said subject a topical pharmaceutical composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1.

Determining the scope and contents of the prior art

Bennett teach a method of treating a condition associated with PKC beta expression comprising administering a composition comprising at least one oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 (PKC beta-1). See claims 70, 76, 86, and 89, for example. Also see claim 90 and Table 3 at page 26, SEQ ID NOs: 25-29.

Ascertaining the differences between the prior art and the claims at issue

Bennett does not explicitly teach that a condition associated with PKC beta expression is depigmentation or hyper-pigmentation as recited in independent claims 38 and 57.

However, Park et al. teach that PKC-β isoforms are closely associated to melanogenesis.

Additionally, Bennett does not explicitly teach that the topical application comprises application to the face, application of a makeup, or application of an SPF protective fluid as recited in dependent claims 61-63. However, Applicant is reminded

that with the decision in *KSR International v. Teleflex Inc. (82 USPQ2d 1385)* it was established that, "Prior art is not limited just to the references being applied, but includes the understanding of one of ordinary skill in the art."

Bennett teaches that the oligonucleotides of their invention are administered topically. Bennett also explicitly teaches:

> "Topical administration may include ointments, lotions, creams, gels, drops, suppositories, sprays, liquids and powders. Conventional pharmaceutical carriers, aqueous, powder or oily bases, thickeners and the like may be necessary or desirable. Coated condoms or gloves may also be useful"

Therefore, using general knowledge, one of ordinary skill in the art would understand that makeup and SPF protective fluid are encompassed in the disclosure of ointments, lotions, creams, etc. as taught in Bennett.

Bennett also does not explicitly teach administering an active agent selected from substances that inhibit the activity of tyrosinase. However, Park et al. teach that inhibition of PKC-β inhibits tyrosinase activity. Therefore, oligonucleotides capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 (PKC beta-1) and other PKC-β inhibitors, such a cyclosporine A, which is associated with carnitin, as disclosed by Bennett would be expected to inhibit tyrosinase activity, absent evidence to the contrary.

It should be noted that Bennett do not explicitly teach that administration of antisense oligonucleotides targeted PKC-β 1 will result in a method of depigmenting or a method of treating regional hyper-pigmentation as recited in independent claims 38 and 57. However, Applicant is reminded that the burden of establishing whether the

teachings of Bennett would have the additional function of resulting in a depigmenting effect or treating regional hyper-pigmentation, under generally any assay conditions falls to Applicant. Applicant is reminded that the Patent Office is not a research facility. See MPEP 2112.02 which states:

> "[U]nder the principles of inherency, if a prior art device, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art device. When the prior art device is the same as a device described in the specification for carrying out the claimed method, it can be assumed the device will inherently perform the claimed process. *In re King*, 801 F.2d 1324, 231 USPQ 136 (Fed. Cir. 1986)."

In all, Bennett teach a method of treating a condition associated with PKC beta expression comprising topically administering an oligonucleotide that specifically hybridizes with PKC beta. Bennett goes on to teach that the oligonucleotide that specifically hybridizes with PKC beta is specific for PKC beta-1. See Table 3 at SEQ ID NOs: 25-29. Park et al. teach that the expression of PKC-β is associated with human melanogenesis. Therefore, by combining the teachings of Bennett along with Park et al., one of ordinary skill in the art would have been motivated to use oligonucleotides that specifically hybridize with PKC beta to arrive at a method of depigmenting or a method of treating regional hyper-pigmentation, which is Applicant's invention, absent evidence to the contrary.

Resolving the level of ordinary skill in the pertinent art

The level of ordinary skill in the pertinent art is considered to be high, being a graduate student or post-doctoral fellow in a biological science.

Considering objective evidence present in the application indicating obviousness or nonobviousness

It would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made to devise a method of depigmenting or treating regional hyper-pigmentation comprising topically administering an oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 (PKC beta-1) using the teachings and motivation of Bennett combined with the teachings of Park et al.

One of ordinary skill in the art would have been motivated to devise a method of depigmenting or treating regional hyper-pigmentation comprising topically administering an oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 (PKC beta-1) since Bennett taught that such a method could treat conditions associated with expression of PKC-β and Park taught that PKC-β expression is associated with pigmentation.

One of ordinary skill in the art would have had a reasonable expectation of success of devising a method of depigmenting or treating regional hyper-pigmentation comprising topically administering an oligonucleotide capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 (PKC beta-1) since, at the time of filing, the topical delivery of antisense oligonucleotides was routine and successful in the art. See, for example Brand, RM. (Curr Opin Mol Ther. 2001 Jun;3(3):244-8.)

Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing.

Response to Arguments

In response to this rejection, Applicants first argue that Bennett as evidenced by Lazou may not be relied upon to disclose or render predictable each and every element of independent claims 38 and 57.

This argument has been considered and is moot in view of the fact that a new rejection, with new arguments has been presented on the record. It is noted that the new rejection of record does not include the reference of Lazou.

Applicants secondly argue it is clear that Bennett does not disclose, neither explicitly or inherently, the topical application of antisense oligonucleotides targeting PKC beta 1, and thus does not disclose neither explicitly nor inherently, a depigmenting effect of antisense oligonucleotides targeting PKC beta 1.

This argument has been considered, but is not found persuasive because as discussed *supra*, Bennett teach a method of treating a condition associated with PKC beta expression comprising topically administering an oligonucleotide that specifically hybridizes with PKC beta. Bennett goes on to teach that the oligonucleotide that specifically hybridizes with PKC beta is specific for PKC beta-1. See Table 3 at SEQ ID NOs: 25-29. Park et al. teach that the expression of PKC-β is associated with human melanogenesis. Therefore, by combining the teachings of Bennett along with Park et al., one of ordinary skill in the art would have been motivated to use oligonucleotides that specifically hybridize with PKC beta to arrive at Applicant's invention, absent evidence to the contrary.

It should be noted that Applicants, in their arguments filed May 18, 2010 at page 12 make the following statements, regarding Park et al:

> "Since PKC beta was known to cover two isoforms, the use of the general term "PKC beta" would clearly have been understood by one of ordinary skill in the art as including both isoforms."
>
> "One of ordinary skill in the art would thus derive from Park that both PKC beta 1 and 2 are necessary for pigmentation, and that depigmentation would necessitate the inhibition of both PKC beta 1 and 2."

In agreeing with Applicant's statements, Park et al. teach both PKC beta 1 and PKC beta 2 are necessary for pigmentation and that depigmentation would necessitate the inhibition of both PKC beta 1 and PKC beta 2. Thus, by combining the teachings of Bennett and Park, one of ordinary skill in the art would have used oligonucleotides targeting both PKC beta 1 and PKC beta 2 to arrive at a method of depigmenting human skin or a method of treating hyper-pigmentation, which is Applicant's claimed invention.

While it is noted that independent claims 38 and 57 require the use of an oligonucleotide specifically hybridizable with PKC beta-1, it should also be noted that independent claims 38 and 57 recite, "comprising", which is open-ended language. For more explanation, see MPEP 2111.03 where it states, "The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps". In this instance, the use of an oligonucleotide specifically hybridizable with PKC beta-1 as recited in independent claims 38 and 57 does not exclude the

additional use of an oligonucleotide specifically hybridizable with PKC beta-2 as well, for example.

Applicants thirdly argue that the present application, as well as the article by Lazou, surprisingly demonstrates that the inhibition of PKC beta 1 only is sufficient to inhibit melanogenesis and thus obtain depigmentation.

This argument has been fully considered, but is not found persuasive because first of all, Applicants have never submitted on the record a Rule 132 Declaration or Declaration testimony arguing "surprising" or "unexpected results". Without such a Declaration, the inherent teachings of Bennett would be expected to carry out the functionality of Applicant's claimed invention, absent evidence to the contrary. Applicants are reminded that mere arguments or conclusory statements by the Attorney are insufficient to satisfy Applicant's burden of showing surprising results.

Second, it should be noted that all of the claims, with the exception of new claim 67, are broad enough to implicitly include modifying the expression of PKC beta 1, along with anything else, including PKC beta 2 expression. For further explanation, see page 11, last paragraph of this Office Action. Therefore, it can only be said that claim 67 is limited to the inhibition of PKC beta 1 only. However, this claim is not novel because Bennett teaches antisense oligonucleotides targeted specifically to PKC beta 1 only or PKC beta 2 only, and therefore inhibition of one beta isoform over another isoform is obvious in view of Bennett. For further explanation, see Bennett at Table 3, page 26, SEQ ID NOs: 25-29.

The Examiner would like to reintroduce to the record a particular statement that Applicant made in their arguments filed May 18, 2010 at page 14, last paragraph:

> "The teachings of Bennett and Park, may have led one of ordinary skill in the art to use oligonucleotides targeting both PKC beta 1 and 2 (see Bennett, Table 2, page 26), not PKC beta 1 alone to achieve depigmentation as required by claim 67".

However, Applicants should note that Bennett, Table 2, page 26, at SEQ ID NOs: 25-29 provide clear motivation to target PKC beta 1 alone. Furthermore, as discussed *supra*, the claims recite "comprising" language, which is open-ended and does not exclude the additional use of an oligonucleotide specifically hybridizable with PKC beta-2, for example.

Applicants lastly argue that the methods according to the invention advantageously permit depigmentation using specifically PKC beta 1 antisense oligonucleotides, without adversely altering other essential skin functions and thus, for at least this reason, the claims are not obvious in view of the cited prior art.

This argument has been fully considered, but is not found persuasive because it appears that Applicants are arguing against limitations that are not recited in the instant claim(s). Applicant is reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, Applicants arguments regarding methods of using specifically PKC beta 1 antisense oligonucleotides without adversely altering other essential skin functions appear to be misplaced since the claims do not recite or even require that other essential skin functions are not inhibited or hampered.

In view of the foregoing, when all the evidence is considered, the totality of the rebuttal evidence of non-obviousness fails to outweigh the evidence of obviousness made of record. Thus, it is maintained that the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was filed.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached from 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

June 10, 2010
/Terra Cotta Gibbs/